

Refractory cutaneous Crohn's disease of the external genitalia in a female

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Abstract

Cutaneous lesions as a part of Crohn's disease (CD) may occur as a totally separate entity without the involvement of the gastrointestinal tract, in which case it is termed as metastatic CD. A 23-year-old female presented with complaints of vulvar swelling and multiple, oval-linear, typical knife cutting deep ulcers on the perineal folds. Biopsy showed epithelioid cell granuloma in the dermis. Differential diagnosis included cutaneous tuberculosis, sarcoidosis, deep fungal infection, and CD of the vulva. A diagnosis of CD was made by the exclusion. The patient was earlier treated with oral steroids, antibiotics, antituberculosis treatment, and azathioprine but showed only mild improvement. Therefore, the condition was regarded as a refractory one. The patient showed significant improvement after six cycles of adalimumab.

Key words: Crohn's disease, granuloma, vulva

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INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory bowel disease of unknown pathogenesis in which there is the development of granulomas and ulcers in the bowel. It can involve any section of the bowel, terminal ileum being the most common. Cutaneous lesions may parallel gastrointestinal (GI) disease activity or may occur as a totally separate entity, in which case it is called as metastatic CD. Gynecologic involvement is infrequent, diverse, and often difficult to diagnose. Vulvar involvement due to CD is an extremely rare condition, with only a few reported cases.^[1] Till now, only about 130 cases have been reported in literature.

CASE REPORT

A 23-year-old married female presented to our outpatient department with complaints of swelling of the vulva and ulcers on the perineal folds for 5 years. The swelling started in 2011 during 1st trimester of gestation, which was gradually progressive (1–5 cm in size). Few painless ulcers developed on the inner aspect of both thighs after 1 year, which gradually increased in number and size. Gradually, she developed pain in the perineum. There was no history of preceding fever, chronic cough, weight loss, oral ulcers, loose stool, and blood in stool. She gave a history of cesarean section, which was performed due to genital prolapse. Then, she was operated for prolapse, and later, biopsy was taken from the swelling to rule out postoperative lymphangioma. The biopsy showed nonspecific granulomas and chronic infiltrates. She was started on oral azathioprine, antibiotics, metronidazole, and steroids with some improvement in groin ulcers and a decrease in vulvar edema and induration. She was on and off treatment for past 3 years with partial relief at best. Meanwhile, she took antituberculosis treatment for 3 months from the gynecology department of a tertiary hospital but did not show any improvement.

The condition worsened, and the patient presented in our OPD with complaints of vulval swelling, fissuring, and typical “knife-cut” ulcers, as shown in Figure 1.

On examination, an irregular firm, lobulated swelling arising from the vulva was appreciated. There were multiple, oval to linear, typical knife cutting deep ulcers with well-demarcated margins, of size varying from 0.5 to 5 cm. The ulcers were tender and showed fresh bleeding.

We repeated a biopsy which showed epithelioid cell granuloma in the dermis with dense chronic inflammatory infiltrate comprising lymphocytes and plasma cells, as shown in Figure 2. Special stains for acid-fast bacillus and reticulin were noncontributory. Our differential diagnosis at this stage included vulvar CD, cutaneous tuberculosis, sarcoidosis, deep fungal infection, and lymphogranuloma venereum.

Colonoscopic biopsy was done from the terminal ileum, which showed only mild inflammatory changes without any features of granulomatous disease. Colonoscopy was normal. Anti-neutrophil cytoplasmic antibody (both p ANCA and c ANCA) and anti-saccharomyces cerevisiae antibodies were negative. Routine hematological investigations and angiotensin-converting enzyme levels were within the normal range. Hepatitis B surface antigen, enzyme-linked immunosorbent assay for HIV, and Venereal Disease Research Laboratory test were negative. Tissue fungal culture was negative. The chest X-ray was normal. Magnetic resonance imaging of the pelvis showed vulvar edema with soft-tissue thickening within superficial subcutaneous layer extending up to the perineum likely inflammatory. In view of the clinical and histopathological features and all other investigations, a diagnosis of CD of the external genitalia was made by the exclusion.

In view of the previous nonresponse, we planned to start biologic therapy in form of injection adalimumab 160 mg (8/8/16)–80 mg (22/8/16)–40 mg (6/9/16) s/c at an interval of 2 weeks for 1 year, along with azathioprine 50 mg bid.

There was significant healing of the ulcers after six cycles of adalimumab, as shown in Figure 3.

DISCUSSION

Cutaneous manifestations occur in 22%–44% of patients with CD.^[2] Three distinct patterns of cutaneous involvement are observed in CD. Direct extension from the bowel to perineal skin, stomal sites, or lips is the most common cutaneous presentation. The second pattern includes extraintestinal cutaneous conditions associated with CD, such as pyoderma gangrenosum, erythema nodosum, and erythema multiforme.^[3] The third pattern is metastatic or isolated CD arising at sites discontinuous from the GI tract. The exact pathogenesis of metastatic CD is unknown, although it has been proposed that a T-lymphocyte-mediated type IV reaction could be partially responsible.^[4] The disease was first described by Parks *et al.* in 1965.^[5] It can present as cutaneous ulcerations, plaques, papules or nodules over skin folds, the inframammary area, limbs, penis, vulva, trunk, or face.^[6] Cutaneous lesions are usually in the inguinal and perineal areas because they are areas of increased moisture.^[7] A retrospective review by Ploysangam *et al.* of 80 cases of metastatic CD demonstrated that 56% of women had gynecological involvement.^[8]

As such, there is no definite curative treatment for metastatic CD. Many treatment modalities have been tried such as topical, intralesional, systemic steroids, sulfasalazine, mesalamine, oral metronidazole, hyperbaric oxygen,^[9] and antitumor necrosis factor-alpha antibodies (infliximab).^[10] Adalimumab is found to be effective in achieving short-term and long-term remission



Figure 1: Swelling rising from vulva, asymmetric, firm-lobulated swelling. Multiple, oval to linear, typical knife cutting deep ulcers with well-demarcated margins of size varying from 0.5 to 5 cm

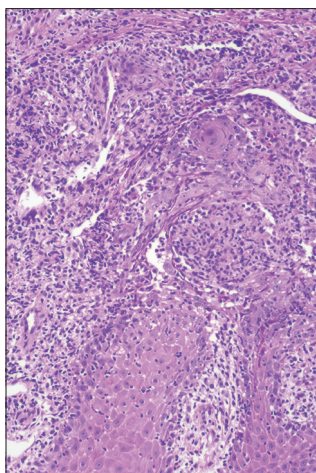


Figure 2: Histopathology showing epithelioid cell granuloma and inflammatory cells

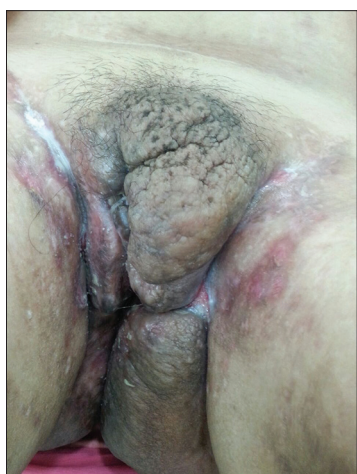


Figure 3: Significant healed ulcers after six cycles of adalimumab

and complete fistula healing in CD.^[11] Now, we have considered it to be used in this case. There are reports of successful use of adalimumab in treating metastatic CD.^[12] Advanced cases may require vulvectomy. Werlin *et al.* have reported that vulvar ulcers may precede intestinal manifestations by up to 18 years.^[13] Therefore, chronic vulvar ulcers require a thorough long-term follow-up.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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